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# Cost-Effectiveness of Sacral Neuromodulation Compared to Botulinum Neurotoxin A or Continued Medical Management in Refractory Overactive Bladder

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## ABSTRACT

### Keywords:

Sacral neuromodulation  
Refractory overactive bladder  
Cost-effectiveness  
QALY  
Budget impact

**Objectives:** This study assessed the cost-effectiveness and health-care budget impact of sacral neuromodulation (SNM) in refractory idiopathic OAB-wet patients in Spain.

**Methods:** A 10-year Markov analytic model was developed to estimate quality-adjusted life-years (QALYs) gained and incontinence episode avoided associated with SNM therapy compared with botulinum neurotoxin A (BoNT-A) or continued optimized medical treatment (OMT).

**Results:** At 10 years, the cumulative costs of SNM, BoNT-A, and OMT were €29,166, €29,458, and €29,370, respectively, whereas the QALYs for SNM, BoNT-A, and OMT are 6.89, 6.38, and 5.12, respectively. Consequently, incremental cost-effectiveness ratios (ICERs) for SNM demonstrate that although the initial costs for SNM are higher than those for the other treatments, decreasing follow-up costs coupled with consistently greater effectiveness in the long term make SNM the economically dominant option at 10 years. Sensitivity analyses suggest that 99.7% and 99.9% (for SNM vs. BoNT-A and OMT, respectively) of the 1000 Monte Carlo iterations fall within the €30,000 cost-effectiveness threshold, considered to be acceptable in Spain. The 10-year incremental cost per incontinence episode avoided for SNM also makes this therapy the dominant option compared to BoNT-A or OMT. Additionally, the estimated budget impact of the gradually increased referral for SNM for the management of OAB patients in Spain is small.

**Conclusions:** As a treatment option for refractory idiopathic OAB, at 10 years, SNM provides a considerable possibility of symptom and quality-of-life improvement and is cost-effective compared to BoNT-A or continued OMT.

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## Introduction

### Epidemiology and burden

Overactive bladder (OAB) is a chronic condition characterized by urinary symptoms of urgency and frequency and with (i.e., OAB wet) or without urinary urge incontinence [1]. These symptoms can be distressing and socially disruptive to patients, causing significant impairment to their health-related quality of life (HRQoL) [2]. In Spain, the prevalence of symptoms suggestive of OAB is estimated to be 19.9% in the adult population of age 40 years and older and particularly high in women (25.6%) [3]. OAB-related direct costs incurred by the Spanish health-care system are estimated to exceed €700 million, and direct annual per-patient costs are estimated to be as high as €550 per patient; the largest proportion of these costs are attributed to the use of incontinence pads [4].

### OAB management pathways

In line with international (International Consultation on Incontinence) treatment guidelines, first-line management for OAB in Spain involves antimuscarinic agents [5]. Clinical trials show some degree of improvement with antimuscarinic agents; however, a high proportion of patients (25%–40%) remain refractory to treatment [6]. Although many refractory patients cease drug treatment [7], a proportion continues with drugs in combination with pad use for several years, undergoing numerous drug switches [8] before eventually embarking on alternative treatment strategies. Sacral neuromodulation (SNM) therapy and botulinum neurotoxin A (BoNT-A) are the less invasive treatment options for patients who are refractory to antimuscarinic agents.

Clinical benefits of SNM therapy are obtained from the electrical impulses generated by an implanted neurostimulator and delivered via a conducting electrode to one of the sacral nerves involved in control of urinary function. Compared to other modalities such as augmentation cystoplasty, implantation of the neurostimulator is a minimally invasive procedure that is performed after a successful test to screen suitable patients. The

test is an effective predictor of success before the fully reversible surgical implantation. Results of short- and long-term clinical studies of SNM demonstrate high rates of clinical success, defined as a significant reduction in voiding-related symptoms, voided volume, and the number of pads used daily and improvement in health-related quality of life (HRQoL) [9–12].

Injection of the bladder wall with BoNT-A, although currently not licensed for use for the idiopathic OAB indication Europe, is often used to treat refractory idiopathic OAB in Spain. Multiple injections of minute doses in the bladder wall reduce neuronal activity and decrease detrusor pressure. Repeat administration, however, is required to maintain symptomatic improvement as the effect of BoNT-A wears off over time [13]. Although results of short-term clinical trials demonstrate the effectiveness of BoNT-A, further studies are needed to demonstrate the long-term efficacy and safety of repeat injections.

### Objectives

Given that OAB is a chronic condition, our objective was to assess the long-term cost-effectiveness of treatment with SNM therapy in refractory idiopathic OAB-wet patients, from the Spanish National Health Service (NHS) perspective, compared to repeat BoNT-A injections or optimized medical treatment (OMT) consisting of continued drug and pad use. The potential budget impact to the Spanish NHS for providing SNM to an increased number of Spanish OAB patients was also measured.

## Materials and methods

### Study design

The cost-effectiveness analysis (CEA) was evaluated using a decision analytic model constructed and analyzed with Microsoft Excel 2003 spreadsheet software (with Visual Basic programming), which is a widely used and transparent tool to develop economic models [14].

The model, which reflected international OAB management guidelines [15,16], simulated a hypothetical cohort of OAB pa-

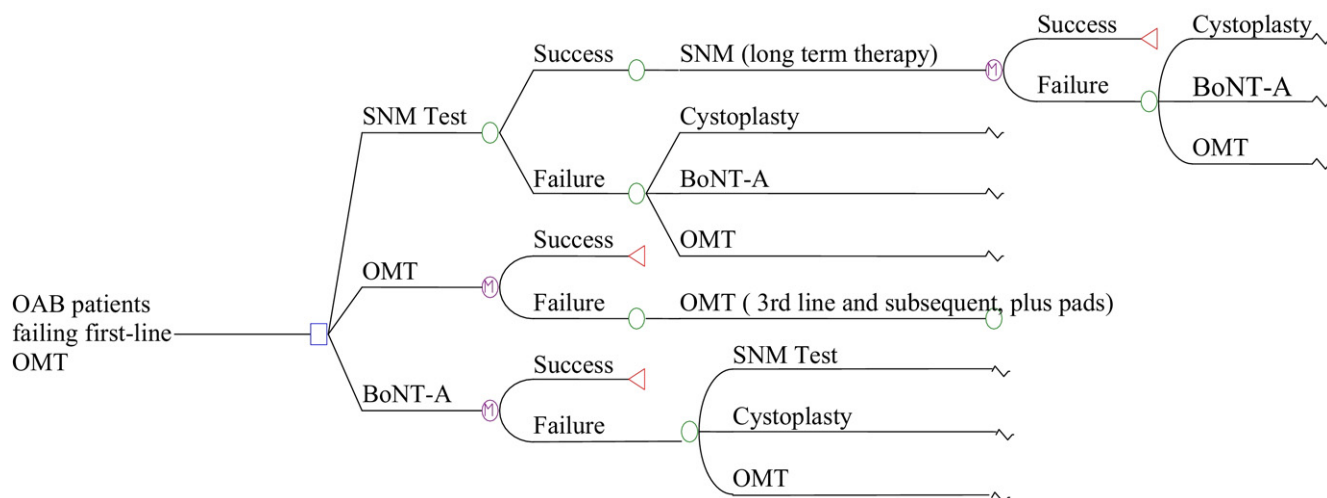


Fig. 1 – Model diagram.

**Table 1 – Treatment transition rates\*.**

After failure of	Next treatment Line			
	SNM test and permanent implant, %	BoNT-A, %	Cystoplasty, %	OMT, %
SNM test and permanent implant	—	77	5	18
BoNT-A	79	—	5	16
OMT	—	—	—	100

BoNT-A, botulinum neurotoxin A; OMT, optimized medical treatment; SNM, sacral neuromodulation.  
 \* Proportion of patients receiving the next available treatment following a failure of treatment as listed in first left-hand-side column.

tients through three alternative treatment pathways (Fig. 1) over a 10-year time frame: 1) SNM therapy involving test and permanent implant, 2) BoNT-A injections, or 3) continued OMT (drugs and pad use). A Markov approach was used to analyze the long-term prognosis of refractory idiopathic OAB patients after failure with first-line OMT. For chronic diseases such as OAB, Markov models offer advanced decision tools to study health states that recur and change over a long period of time, particularly when they cannot be captured within clinical studies; thus enabling the simulation of health outcomes and costs using long-term data gathered from multiple sources.

The 10-year model was divided into 12-month cycles. During each cycle, patients remained in the same treatment as the previous cycle unless the treatment outcome (defined as success or failure) was a failure. When a failure occurred, patients switched to another treatment according to the treatment transition rates specified by an expert panel (Table 1). After 10 cycles, cumulative costs, effectiveness measured as quality-adjusted life years (QALYs), and the number of incontinence episodes estimated by ascribing a given number of incontinence episodes to success and failure [11] were calculated. These estimates were then used to derive an incremental cost-effectiveness ratio (ICER), the ultimate measure of interest in a CEA, which is defined as the ratio of the difference in costs and the difference in outcomes for one intervention compared to another. The ICERs in the current study are expressed as the incremental cost per QALY gained and incremental cost per incontinence episode avoided at 10 years for SNM compared to the other treatment pathways. In line with current recommendations for CEA conducted in European settings, a discount rate of 3% per annum was applied to the ICER estimates to account for the current value of the future stream of costs and effectiveness [17]. An expert panel of five experienced urologists from four Spanish hospitals developed assumptions of treatment pathways; provided rates of resource use, treatment transitions, and adverse events; and validated effectiveness outcomes. The

panel was consulted via two focus group meetings and structured interviews.

The model also facilitated the budget impact analysis, which evaluated the direct cost impact on the Spanish NHS in four consecutive years if the number of women treated with SNM therapy increased.

### Treatment outcomes

The outcomes of OAB in the treatment arms of the model were classified as success ( $\geq 50\%$  improvement in incontinence symptoms) or failure ( $< 50\%$  improvement in incontinence symptoms).

Treatment outcomes (Table 2) were primarily based on a literature review of evidence published within databases including Cochrane, Centre for Reviews and Dissemination, PubMed, the CEA Registry, and the Spanish Medical Index. The search strategy identified studies that were published in English or Spanish that analyzed OAB clinical or HRQoL outcomes or resource utilization and in relation to SNM and the comparators in the treatment of OAB. When published evidence was lacking, expert panel input was the source for model data.

In the SNM arm of the model, treatment outcomes for the definitive implant of SNM up to 5 years were based on combined clinical trial data of two implantation methods [11–13,18]. It was assumed that patients first undergo screening for an average duration of 3.2 weeks (based on expert opinion), resulting in a positive response rate of 80% [18,19]. Thus, the first year treatment success rate of 90% (Table 2) is relevant to the proportion showing a positive response to screening.

The clinical outcomes for BoNT-A in the first year were based on results observed in one-injection cycle trials in idiopathic OAB [12,20]. The expert panel provided additional input on treatment patterns, as follows: 1) Repeat injections at a 100-U dose were administered every 9 months for BoNT-A responders (in 20% of patients in whom treatment failed in the first cycle, the dose was increased to

**Table 2 – Treatment outcomes.**

Treatment	1 year, %	2 years, %	3 years, %	4 years, %	5 years, %	7 years, %	10 years, %
SNM	90	86	82	78	75	75	75
BoNT-A	80	74	68	63	59	54	50
OMT	4	4	4	4	4	4	4

BoNT-A, botulinum neurotoxin A; OMT, optimized medical treatment; SNM, sacral neuromodulation.

200 U). 2) Successive outcomes beyond the first year were estimated by applying a yearly treatment dropout rate of 7.5% to account for the treatment efficacy waning over time,

discontinuation due to adverse events, or a search for a definitive solution as observed in patients with detrusor overactivity [21].

**Table 3 – Treatment costs.**

Treatment	Costs				
	Preprocedure (e.g., lab tests, radiography), €	Procedure (including device or drug), €	Adverse events (per annum costs), €*	Follow-up (per 3 months) Up to first 3 months, €    After first 3 months, €	Follow-up after treatment failure, €
SNM test	558	2781	—	94	867
SNM	102	9734	436	166	98
BoNT-A (costs repeated every 9 months)	572	1192	132	500	233
OMT	—	First-line drug cost: €153 Second-line drug cost: €189 Third-line drug cost: €20 Fourth-line drug cost: €51	302	707	707
Cystoplasty	736 (includes cystoscopy)	2783	415	4249	415
Major adverse events considered					
SNM	Reoperation: 8% <sup>a</sup> Lead- or IPG-related issues: 4%–5% <sup>a</sup> Surgical site/device infection: 3% <sup>b</sup>				
BoNT-A	Partial urinary retention: 45% <sup>c</sup> Acute urinary retention: 23% <sup>d</sup> Dysuria: 24% <sup>e</sup> Urinary tract infection: 24% <sup>f</sup>				
OMT	Urinary tract infection: 11.5% <sup>g</sup> Xerostomia: 16% <sup>h</sup> Risk of fracture: 8% <sup>i</sup> Constipation: 7% <sup>h</sup>				
Cystoplasty	Urinary tract infection: 24% <sup>j</sup> Calculus formation: 24% <sup>k</sup> Bladder perforation: 5% <sup>l</sup>				

BoNT-A, botulinum neurotoxin A; IPG, implantable pulse generator; OMT, optimized medical treatment; SNM, sacral neuromodulation.

<sup>a</sup> Kessler TM, Buchser E, Meyer S, et al. Sacral neuromodulation for refractory lower urinary tract dysfunction: results of a nationwide registry in Switzerland. *Eur Urol* 2007;51(5):1357–63.

<sup>b</sup> van Kerrebroeck PE, van Voskuilen AC, Heesakkers JP, et al. Results of sacral neuromodulation therapy for urinary voiding dysfunction: outcomes of a prospective, worldwide clinical study. *J Urol* 2007;178(5):2029–34.

<sup>c</sup> Brubaker L, Richter HE, Visco A, et al. Pelvic Floor Disorders Network. Refractory idiopathic urge urinary incontinence and botulinum A injection. *J Urol* 2008;180(1):217–22.

<sup>d</sup> Werner M, Kuschel S, Schmid DM, Schuessler D. Efficacy of botulinum toxin A in the treatment of female idiopathic detrusor overactivity incontinence: long-term results of a prospective nonrandomized study. *Eur Urol Suppl* 2006;5(11):685–90.

<sup>e</sup> Kuo HC. Comparison of effectiveness of detrusor, suburothelial and bladder base injections of botulinum toxin A for idiopathic detrusor overactivity. *J Urol* 2007;178:1359–63.

<sup>f</sup> Sahai A, Khan Ms, Dasgupta P; the GKT Botulinum Study Group. Efficacy of botulinum toxin-A for treating idiopathic detrusor overactivity: results from a single center, randomized, double-blind, placebo controlled trial. *J Urol* 2007;177:2231–6.

<sup>g</sup> Klotz T, Brüggengjürgen B, Burkart M, Resch A. The economic costs of overactive bladder in Germany. *Eur Urol* 2007;51(6):1654–62.

<sup>h</sup> Staskin D, Sand P, Zinner N, Dmochowski R, for the Trosipium Study Group. Once daily trosipium chloride is effective and well tolerated for the treatment of overactive bladder: results from a multicenter phase III trial. *J Urol* 2007;178:978–83.

<sup>i</sup> Brown JS, Vittinghoff E, Wyman JF, et al. Urinary incontinence: does it increase risk for falls and fractures? Study of Osteoporotic Fractures Research Group. *J Am Geriatr Soc* 2000;48:721–5.

<sup>j</sup> McDougal WS. Metabolic complications of urinary intestinal diversion. *J Urol* 1992;147(5):1199–208.

<sup>k</sup> Blyth B, Ewalt DH, Duckkett JW, Snyder HM III. Lithogenic properties of enterocystoplasty. *J Urol* 1992;148:575.

<sup>l</sup> Bauer SB, Hendren WH, Kozakewich H, et al. Perforation of the augmented bladder. *J Urol* 1992;148:699–703.

**Table 4 – Cost-effectiveness analyses.**

Treatment	Improvement, %	Total per-patient costs, €	QALYs	ICER (cost/QALYs gained), €	Episodes	ICER (costs/episode avoided), €
5 years						
SNM	72.1	19,156	3.69		9561	
BoNT-A	68.6	18,235	3.45		9790	
OMT	0.0	15,932	2.75		16,529	
Incremental: SNM vs. BoNT-A year 5		921	0.24	3775	229	4.02
Incremental: SNM vs. OMT year 5		3223	0.94	3412	6968	0.46
7 years						
SNM	68.8	26,019	5.03		12,976	
BoNT-A	62.9	22,597	4.68		13,389	
OMT	0.0	21,593	3.74		22,486	
Incremental: SNM vs. BoNT-A year 7		3422	0.35	9830	413	8.29
Incremental: SNM vs. OMT year 7		4426	1.29	3433	9509	0.47
10 years						
SNM	62.1	29,166	6.89		17,765	
BoNT-A	55.2	29,458	6.38		18,498	
OMT	0.0	29,370	5.12		30,787	
Incremental: SNM vs. BoNT-A year 10		–292	0.51	Dominant	733	Dominant
Incremental: SNM vs. OMT year 10		–204	1.77	Dominant	13,021	Dominant

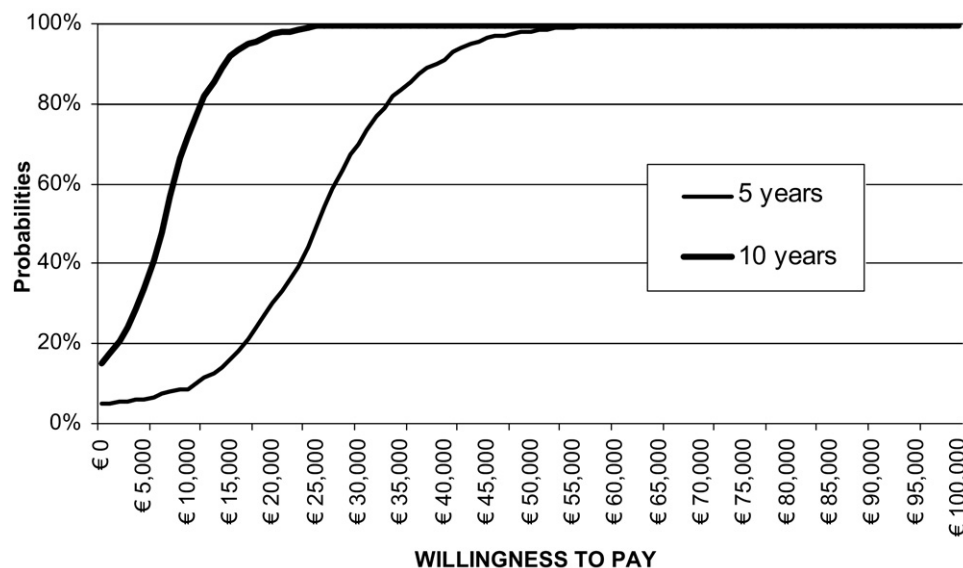
BoNT-A, botulinum neurotoxin A; ICER, incremental cost-effectiveness ratio; OMT, optimized medical treatment; QALY, quality-adjusted life-year; SNM, sacral neuromodulation.

Treatment effects for OMT were based on 6-month treatment data in refractory patients who continued treatment [9]; this rate was maintained throughout the period. Augmentation cystoplasty (i.e., surgery to increase bladder capacity) was included as a treatment option after failure of SNM or BoNT-A, as shown in Fig. 1).

### Qalys

To measure the impairment to patient HRQoL [2] due to OAB, QALY weights were assigned to the health outcomes of treatment success or failure. QALYs are a measure of the length of

life adjusted for HRQoL related to a disorder, in addition to health benefits associated with treatment. Thus, 1 year of perfect health is equivalent to 1.0 QALY. The QALY weights applied to the current model were derived from the literature, because none of the SNM trials directly measured utilities associated with OAB outcomes. Thus, the QALY weights in the current analysis were defined as 0.793 for treatment success (continence) and 0.573 for treatment failure (incontinence), as estimated from a synthesis of Basque general population utilities [22] and from Wu et al. [23]. Although we believe that the same sources for the QALYs would have been better for model validity, the utility values from Wu et al., which

**Fig. 2 – CE acceptability curve for SNM versus BoNT.**



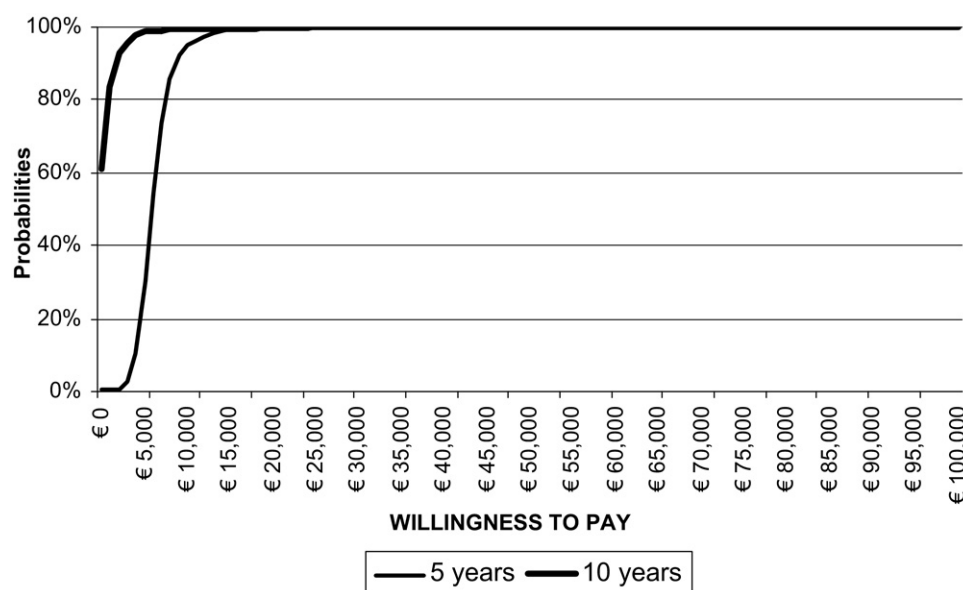


Fig. 3 – CE acceptability curve for SNM versus OMT.

were 0.951 for continence and 0.730 for urinary incontinence, were considered to be very high for Spain, as suggested by the Basque general population utility of 0.793. Thus, we applied the net disutility of 0.221 of Wu et al. associated with moving from a continent to an incontinent health state to the Basque general population utility scores to obtain the respective utilities for the treatment outcomes in the model; these were deemed to provide conservative estimates of QALYs after OAB treatment. Cumulative QALYs were then derived for each treatment arm at a given time-frame of analysis.

### Cost inputs

Because the perspective of the model was from the Spanish NHS, the analyses considered direct health-care costs only, and these were expressed in 2008 Euro values. Costs comprised health-care resources used at treatment initiation (pre-procedure costs), during treatment (procedure and drug costs), during follow-up, for adverse events, and after treatment failure (Table 3). Estimates of the units of health-care

resources for OMT were obtained from published sources [4,24], whereas other estimates were provided by expert opinion. Unit costs were obtained from the 2008 e-Salud Spanish health-care cost database, and the Spanish Ministry of Health. SNM device costs were based on InterStim and provided by Medtronic. SNM costs also included device and implant costs and, due to device longevity, costs of one neurostimulator battery replacement at year 7. BoNT-A drug costs were based on a 100-U dose of Botox.

### Sensitivity analyses

Probabilistic sensitivity analyses, accounting for the inherent uncertainty in the parameters of the economic evaluation, were conducted via Monte Carlo simulations with 1000 iterations for each treatment. The main uncertainty stems from clinical trial heterogeneity in the definition and measures of symptom improvement, length of follow-up, patient populations, and the lack of long-term data, which thus required treatment outcome assumptions beyond 5 years for SNM, beyond 1 year for BoNT-A, and beyond 6 months for OMT. Hence,

Table 5 – Incontinence disutility sensitivity analysis.

Disutility value	ICER, €					
	SNM vs. BoNT-A			SNM vs. OMT		
	5 years	7 years	10 years	5 years	7 years	10 years
0.293	2834	7381	Dominant	2562	2578	Dominant
0.243	3418	8900	Dominant	3089	3109	Dominant
0.220	3775	9830	Dominant	3412	3433	Dominant
0.193	4303	11,206	Dominant	3889	3914	Dominant
0.143	5807	15,124	Dominant	5249	5282	Dominant
0.093	8930	23,255	Dominant	8071	8122	Dominant

BoNT-A, botulinum neurotoxin A; ICER, incremental cost-effectiveness ratio; OMT, optimized medical treatment; SNM, sacral neuromodulation.

fixed probability distributions were selected (log-normal distribution for costs, normal distribution for resource use, and beta/Dirichlet distribution for probabilities), and the parameters of each distribution were estimated using the SD and 10% increment/decrement of the mean of primary data. Data that were estimated or obtained via expert opinion underwent variation ranging from 15% to 200%. Two separate deterministic sensitivity analyses were also performed. The first analysis examined the effect of variation in treatment parameters based on a recent study of a 200-U BoNT-A dose; this included reinjection every 14 months, an 8% dropout rate, adverse events including 43% self-catheterization and 15% acute urinary retention [25]. A further sensitivity analysis examined the effect of a variation to the disutility value of 0.22 applied to the estimation of QALYs related to OAB treatment outcomes.

## Results

### Cost-effectiveness

Results of the CEA (Table 4) indicate that, from a medium-term perspective, ICER estimates for SNM are €3775 compared to BoNT-A and €3412 compared to OMT at 5 years, whereas ICERs at 7 years (which accounts for an SNM generator replacement) are €9830 and €3433 compared to BoNT-A and OMT, respectively. These results suggest cost-effectiveness for SNM in the medium-term given that the ICERs are well within the €30,000 cost-effectiveness threshold, which is deemed as efficient in Spain [26]. Additionally, at 10 years, the cumulative costs of SNM, BoNT-A, and OMT are €29,166, €29,458, and €29,370, respectively, with cu-

**Table 6 – Budget impact analyses.**

Target population and incremental potential of SNM				
Population (women > 45 years of age) <sup>a</sup>	10,309,538			
Prevalence of OAB in Spain (in women > 45 years of age), % (no.)	17.37 <sup>b</sup> (1,790,338)			
OAB with urge incontinence	68 <sup>c</sup> (1,217,430)			
Idiopathic OAB wet	90 <sup>c</sup> (1,095,687)			
Diagnosed	52 <sup>c</sup> (569,757)			
Treated	16.7 <sup>c</sup> (95,149)			
In whom OMT failed	33 <sup>d</sup> (31,399)			
Target patient population = 31,399: current scenario*				
	OMT	Cystoplasty	SNM	BoNT-A
Patient treatment rates by therapy, %	89.7	0.3	3.3	6.7
	Budget impact			
Annual incidence of OAB	2%			
	1 year	2 years	3 years	4 years
Patients with OAB who fail first-line OMT	31,399	32,059	32,732	33,419
Patients with current SNM treatment rates (5.7% based on expert opinion)				
OMT	28,165	28,704	29,250	29,803
Cystoplasty	94	95	95	95
SNM	1036	1118	1207	1302
BoNT-A	2104	2142	2180	2219
Patients with increased SNM treatment rates (11.4% based on expert opinion)				
OMT	28,114	28,593	29,067	29,533
Cystoplasty	93	91	90	88
SNM	1095	1246	1417	1612
BoNT-A	2098	2129	2158	2187
Budget impact with current SNM treatment rates, €	15,154,472	18,517,065	20,424,484	122,305,077
Budget impact with increased SNM treatment rates, €	15,398,301	19,889,765	21,872,397	123,828,982
Net impact, €	243,829	1,372,700	1,447,913	1,523,906
% Net impact	0.21	1.16	1.20	1.25

BoNT-A, botulinum neurotoxin A; OAB, overactive bladder; OMT, optimized medical treatment; SNM, sacral neuromodulation.

<sup>a</sup> Spanish Statistics Institute. Last population analysis, 2008.

<sup>b</sup> Martínez Agulló E, Ruiz Cerdá JL, Gómez Pérez L, et al; Grupo de Estudio Cooperativo EPICC. Prevalencia de incontinencia urinaria y vejiga hiperactiva en la población española: resultados del estudio EPICC [Prevalence of urinary incontinence and hyperactive bladder in the Spanish population: results of the EPICC study]. *Actas Urol Esp* 2009;33(2):159–66.

<sup>c</sup> Castro D, Espuña M, Prieto M, Badia X. Prevalencia de vejiga hiperactiva en España: estudio poblacional [Prevalence of overactive bladder in Spain: a population-based study]. *Arch Esp Urol* 2005;58(2):131–8.

<sup>d</sup> Wein AJ. Diagnosis and treatment of the overactive bladder. *Urology* 2003;62(5 Suppl 2):20–7.

\* Expert panel.

mulative QALYs of 6.89, 6.38, and 5.12. Thus, the relative cost savings for SNM, coupled with its enhanced outcomes compared to either treatment, demonstrate that SNM is the economically dominant treatment option in a 10-year time frame. Furthermore, ICERs for incontinence episode avoided at 10 years also demonstrate economic dominance for SNM compared to BoNT-A and OMT.

### Sensitivity analyses

The 1000 incremental CEA results obtained in the probabilistic sensitivity analyses are plotted in acceptability curves of SNM versus the comparative treatment (Figs. 2 and 3). These represent the probabilities that the treatment is cost-effective at different threshold values of cost-effectiveness, based on the CEA conducted. Given an acceptable cost-effectiveness threshold of €30,000 in Spain [26], the analyses suggest that 99.7% of the 1000 simulations fall below the threshold when comparing SNM to BoNT-A (Fig. 2). When comparing SNM to OMT, 99.9% of the simulations fall within the acceptable threshold (Fig. 3).

Similarly, deterministic sensitivity analyses, applying the different BoNT-A treatment parameters from a recent trial [25] also demonstrate the robustness of the inputs, obtaining similar results of dominance at 10 years and cost-effectiveness at 5- and 7-year time frames. When the sensitivity analysis considered net disutility values presented in the other studies of incontinence symptom impact [27,28], the cost-effectiveness of SNM compared to BoNT-A and OMT remained (Table 5.)

### Budget impact

An estimation of the target population of female adult patients older than 45 years of age for the budget impact analysis is shown in Table 6. The estimated target population suitable for a test trial with SNM is 31,000 patients. With an annual OAB incidence rate of 2%, the estimated net impact of increasing the treatment rate of SNM by 11.4% in the current management of OAB patients in Spain seems to be small, representing an increment of 0.2% to 1.25% only in total costs, respectively, from year 1 to year 4 (Table 6 and Fig. 4).

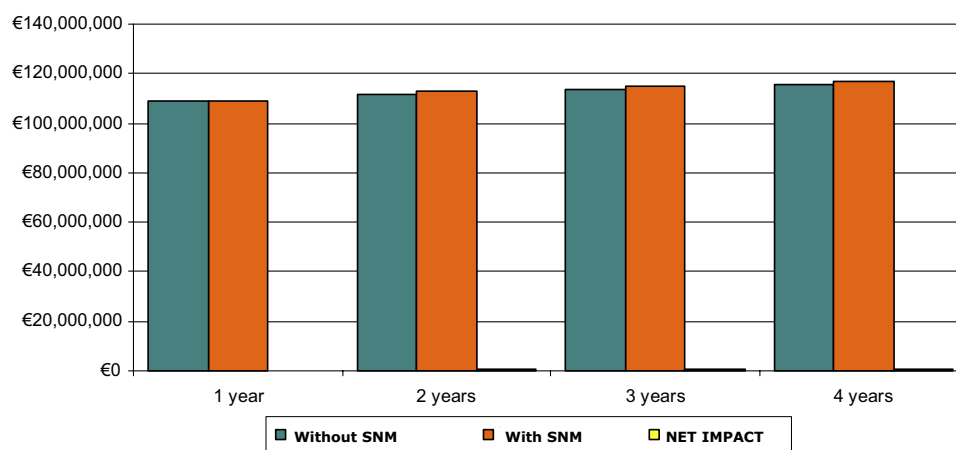


Fig. 4 – Potential budget impact of introducing SNM to female OAB patients in Spain.

## Discussion

Idiopathic OAB causes appreciable burden to patients' HRQoL and results in significant costs related to pad use and urinary tract infections [2,4]. Moreover, health-care practice indicates that a high number of drug refractory patients continue with several oral medication switches despite experiencing no lasting improvement. Given the availability of multiple OAB therapies that can improve patient symptoms, it is necessary to assess their clinical and economic value to aid health-care decision making in the selection of treatment. Because OAB is a chronic condition, any appropriate assessment of treatment must reflect a long-term perspective.

Currently, two publications compare the cost-effectiveness of BoNT-A to that of anticholinergic agents [23] and to SNM [29], which is only present in a 2-year time frame in the US setting. Other analyses [30] comparing BoNT-A, SNM, and augmentation cystoplasty only compared 3-year direct treatment costs. These perspectives are limited because they do not consider treatment outcomes and other longer term cost drivers pertaining to treatment failure and adverse events.

SNM therapy has existed since 1994 for refractory OAB [11]. The treatment is now included in international (ICI) and European (European Association of Urology) guidelines for idiopathic OAB before invasive surgical procedures [15,16]. Until now, the combined clinical and economic value of this technology has not been assessed. The results of the current 10-year study confirm that SNM in Spain is the superior treatment option after first-line medical management fails. The relatively higher initial costs of SNM are offset by the favorable longer term outcomes of symptom and HRQoL improvements and lower annual follow-up costs compared to both BoNT-A and OMT, which require repeat treatment. Apart from yearly follow-up outpatient visits, treatment reintervention is only required every 7 years to replace the depleted neurostimulator battery (cost included in this study). Furthermore, the health-care budget impact of increasing the referral of eligible OAB patients to SNM in Spain seems to be small and affordable in the subsequent 4 years.

Although medical management is the first-line treatment and is not a relevant direct comparator to SNM, the compari-



son in this analysis is relevant given that refractory idiopathic OAB patients in Spain can remain on drug treatment indefinitely (OMT).

Although BoNT-A is not commercially licensed for the treatment of OAB patients, it is routinely used in clinical practice. Several treatments are required during a patient's life time; however, the long-term efficacy and safety trial evidence is limited beyond the administration of the first injection. The lack of a standard treatment protocol among practitioners poses additional challenges [31] to measuring cost-effectiveness from a national perspective. In addition to a base-case treatment protocol provided by expert opinion (100-U dose, reinjection every 9 months, 7.5% dropout rate), a deterministic sensitivity analysis was performed with a different set of variables (200-U dose, reinjection every 14 months, 8% dropout rate). The cost-effectiveness results were similar. Conservative assumptions made in this CEA to estimate the mid- to long-term BoNT-A efficacy mainly account for the patient dropout rate due to reduced efficacy, intolerable adverse events, or the search for a definitive solution.

For SNM, recent technological changes in the screening and implant methods have increased positive screening results [32]. Because there are no long-term clinical data on new implantation methods, the clinical data used to determine SNM treatment effectiveness in the long-term were based on the former implantation method [18] with evidence up to 5 years.

A primary limitation of this CEA is the lack of direct comparative data and long-term evidence from clinical studies comparing the alternative treatments. This subjects the model to uncertainty because treatment outcome assumptions are based on different sources and levels of evidence. Although in the future, comparative and longer term clinical trials showing the efficacy, safety, and impact on HRQoL of SNM and BoNT-A may provide more reliable data to measure the cost-effectiveness of SNM, there is a pressing need to substantiate the long-term cost-effectiveness for mainstream refractory OAB treatments such as SNM and BoNT-A (which is being widely used before its approval for use in idiopathic OAB) with the available evidence base [33] and confirm these results with direct comparative evidence when it is available. These CEA data are also pertinent to the Spanish NHS because the extensive use of BoNT-A in idiopathic OAB patients presenting to their clinical services is nowadays a reality despite the lack of an indication for this use [34]. This was the motivation for the current study. Furthermore, when data limitations such as these do exist, the application of evidence synthesis for indirect comparisons is recognized to fulfill the established international and regional frameworks for rigorous analytical methodology to support clinical decision making [35,36]. Nonetheless, the robust sensitivity analysis applied to handle all the uncertainties of the model indicated a high probability of SNM cost-effectiveness.

## Conclusions

As a treatment option for refractory idiopathic OAB patients, SNM provides a considerable possibility of symptom and

HRQoL improvement and is cost-effective compared to BoNT-A or continued OMT.

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